C. REMARKS

Claims 1-3 and 6-8 have been withdrawn from consideration. Applicants reserve the right to prosecute such claims in a continuing application.

Claims 4 and 5 have been amended. The fact that Claims 4 and 5 have been amended is not to be construed as an admission by Applicants or Applicants' attorneys that such claims, prior to amendment, were unpatentable.

Claims 4 and 5 stand rejected under 35 U.S.C. 102(b) as being anticipated by Lemoli, et. al. as evidenced in Developmental Biology (Page 357). This rejection is respectfully traversed.

The present invention is directed to a method for treating a patient in need of megakaryocytes by administering to the patient isolated and purified human mesenchymal stem cells in an amount effective to produce megakaryocytes. The isolated and purified human mesenchymal stem cells may be administered with $CD34^+$ cells, if desired.

Lemoli discloses the administration of autologous bone marrow transplants to patients suffering from either non-Hodgkin's lymphoma or Hodgkin's Disease. Prior to the administration of the bone marrow transplant, the patients underwent a myeloablative chemotherapy treatment. In addition to the bone marrow transplant, the patients also received G-CSF, or a combination of G-CSF and Interleukin-3.

Lemoli, however, does not disclose or even remotely suggest to one of ordinary skill in the art the isolation and purification of human mesenchymal stem cells from the bone marrow cells, followed by the administration of such isolated human mesenchymal stem cells to the patient. Therefore, Lemoli does not anticipate Applicants' methods as claimed, nor does Lemoli render Applicants' methods as claimed obvious to one of ordinary skill in the art. It is therefore respectfully requested that the rejection under 35U.S.C.102(b) be reconsidered and withdrawn.

Claims 4 and 5 stand rejected under 35 U.S.C.112, first paragraph, because the specification does not reasonably provide enablement for administering only mesenchymal stem cells or mesenchymal stem cells and $CD34^+$ cells alone. This rejection is respectfully traversed.

The Examiner has taken the position that the method to produce specifically megakaryocytes in vivo, by administering mesenchymal stem cells, had not been demonstrated.

In response, Applicants assert that the burden is not upon Applicants to show that the claimed method is effective. Instead, the burden is upon the Examiner to show that the claimed treatment would not be effective. (See In Re Marzocchi, 169 U.S.P.Q.367(C.C.P.A 1971), at 370)

In fact, the Examiner has admitted that mesenchymal stem cells can promote the differentiation of $CD34^+$ cells in vitro. One skilled in the art would expect reasonably that the mesenchymal stem cells, when administered in vivo, would provide for the differentiation of cells into megakaryocytes. The Examiner has provided no evidence, other than speculation, that the administration of isolated human mesenchymal stem cells in vivo would not promote the differentiation of cells into megakaryocytes.

The Examiner also states that the reasons and/or circumstances of a patient in need of megakaryocytes alone are not discussed specifically or defined in the art of record.

In response, the claimed invention is directed to treating patients in need of megakaryocytes. Treatment includes the alleviation of a disease or adverse condition, as well as a cure. Thus, even though some patients may have treatment requirements in addition to megakaryocytes, providing such patients with megakaryocytes still may alleviate the disease or adverse condition, and can be part of an overall treatment regimen. Thus administering mesenchymal stem cells, or a combination of mesenchymal stem cells and $CD34^+$ cells, to a patient receiving chemotherapy, a bone marrow transplant, or a peripheral blood stem cell transplant constitutes a treatment of a patient in need of megakaryocytes even though such patients may require additional therapies. It would be contrary to the interests of justice to require Applicants to limit the scope of their protection to specific patients, whereby one would avoid infringement by treating patients outside the scope of Applicants' claims yet within the broad scope of Applicants' inventive discovery.

The Examiner also states that the term "mesenchymal stem cell" encompasses a stem cell derived from various mesenchymal derived tissues, and because Dexter

states that cells from the spleen, liver, or other tissues do not support hemopoiesis in vitro, the claims are not enabled for all mesenchymal stem cells.

In response, Applicants note that the passage in Dexter referred to by the Examiner states in its entirety that:

"Stromal cells from spleen, liver, or other tissues do not support hemopoiesis in vitro." Nothing in such passage indicates that such cells are mesenchymal stem cells. Thus, the Examiner's position that the term "mesenchymal stem cells" is too broad with respect to the claimed invention is unfounded.

The Examiner also states that all the methods described to restore megakaryocytopoiesis in vivo have relied upon administration of a "stem cell" or "progenitor cell" which is capable of differentiating into a desired cell type, and that to date, there is no report that administration of a "mesenchymal cell" would produce the same effect as a "stem cell" upon administration.

In response, Applicants assert that their claimed invention is directed to treating a patient in need of megakaryocytes by administering to the patient isolated human mesenchymal stem cells, and not a "mesenchymal cell" per se.

The Examiner has provided no evidence, other than speculation, which would indicate to one skilled in the art that one could not restore megakaryocytopoiesis in vivo by administering mesenchymal stem cells to a patient. Such speculation is insufficient under the patent law to support a holding that the claims are not enabled.

The Examiner also has taken the position that there is no working example nor guidance regarding the method of administration of mesenchymal stem cells on megakaryocytopoiesis in vivo.

In response, as stated hereinabove, the Examiner has provided no evidence, other than speculative statements, which would indicate to those skilled in the art that one could not administer mesenchymal stem cells to a patient in vivo in order to provide megakaryocytes to the patient. In addition, the patent law does not require that the specification provide working examples. Thus, the Examiner has not met his burden, under the patent law, to show that the specification does not provide an enabling disclosure.

The Examiner states further that Applicants have defined a potential use of an in vivo method of treatment using mesenchymal stem cells, but essentially have left all of

the work to develop a working method in vivo for any patient in need of megakaryocytes to others.

In response, Applicants assert that the mesenchymal stem cells, or the combination of mesenchymal stem cells and $CD34^+$ cells, may be administered by means known to those skilled in the art. In addition, the Examiner has noted that the differentiation of progenitor cells into megakaryocytes has been achieved, and that explant of bone marrow, in particular the $CD34^+$ hematopoietic stem cells in the marrow, are capable of differentiating into megakaryocytes in vivo. Therefore, one skilled in the art would expect reasonably, based on the above, that one could administer mesenchymal stem cells to a patient, to promote the differentiation of cells into megakaryocytes. Thus, undue experimentation is not required.

The Examiner has stated that the specification is silent with respect to any disease or condition in which only megakaryocytes are required.

In response, Applicants state that, at Pages 1 through 3 of the specification, it is noted that megakaryocytes differentiate into platelets. Thus, a patient in need of platelets could be treated with megakaryocytes. For example, a patient who has a platelet deficiency could benefit from the present invention. Therefore, the Examiner's statement that the specification is silent with respect to any disease or condition in which only megakaryocytes are required is unfounded, and the Examiner has provided no evidence which would indicate to one skilled in the art that such diseases or conditions could not be treated.

For the above reasons and others, the specification provides an enabling disclosure, and it is therefore respectfully requested that the rejection under 35 U.S.C.112, first paragraph, be reconsidered and withdrawn.

In response to the Examiner's statement that the application lacks the necessary reference to the prior application, in the Request for Filing a Continuation Application filed on February 9, 2001, Applicants, in Paragraph 6 of such request, requested that the specification be amended by inserting before the first line the sentence:

--This is a continuation of Application Serial No. 09/316,797, filed May 21, 1999, which is based on U.S. Provisional Application No. 60/086,420, filed May 22, 1998, and U.S. Provisional Application No. 60/108,308, upon which this Application claims priority.--

Therefore, the application includes the necessary reference to the prior application.

For the above reasons and others, this application is in condition for allowance, and it is therefore respectfully requested that the rejections be reconsidered and withdrawn and a favorable action is hereby solicited.

Respectfully submitted

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